REMARKS

Claims 1-4, 6, 8, 9, 12, 15-18, 23-29 and 37 are pending in the present application, with claims 1-4, 6, 8, 9, 12, 23-29 and 37 having been withdrawn from further consideration. By the present Communication, no claims have been added or canceled, and claims 15 and 16 have been amended to define Applicants' invention with greater particularity. Support for the amended claim language may be found in the specification and original claims as filed. Accordingly, claims 15-18 are currently pending.

Rejection Under 35 U.S.C. §101

Applicants respectfully traverse the rejection of claims 15-18 under 35 U.S.C. §101 as allegedly not supported by either a specific and substantial asserted utility or a well established utility. The Examiner alleges that the application does not disclose the biological role or significance of the GDF-12 protein and therefore the specification does not provide a specific substantial and credible utility.

As amended, claims 15-18 are directed to a method of detecting malignant cells. In general, the methods utilize an antibody that specifically binds to GDF-12 in a specimen obtained from a subject, detecting binding of the antibody, and comparing the amount of GDF-12 detected in the sample with an amount in a control specimen, wherein a difference in the sample as compared to control is indicative of malignant cells.

Applicants submit that a method of detecting malignant cells by determining an amount of a protein produced by the cells, is a well established utility that is specific, substantial and credible. The utility is specific in that the specification discloses that GDF-12 is specifically expressed by liver cells and, therefore, provides a specific marker for liver cells (see, for example, Figure 1). The utility also is substantial in that there is a real world value in providing a means to determine whether an abnormal amount of liver cell proliferation is occurring in a subject, as can happen, for example, in a subject with a hepatoma or a hepatocarcinoma.

Furthermore, the utility is credible because one skilled in the art would believe, for example, that an increased level of GDF-12 expression in liver cells would be associated with abnormal liver cell proliferation and malignancy because increase liver cell proliferation would be expected to produce more GDF-12.

By analogy, Applicants point out that the levels of various proteins, including cyclin D1, PCNA, prothrombin, and others are known to correlate with the level of proliferation of cells producing these proteins and that the detection of such proteins has been used in diagnostic procedures. Further in this respect, Applicants point out that the level of prostate-specific antigen (PSA) in the blood was well recognized as a diagnostic marker of a prostate cell proliferative disorder, even though the function of PSA was not known. Thus, even where the function of a protein such as PSA was not known, it was recognized that the level of PSA was increased above normal in benign prostate hyperplasia and in prostate carcinoma, presumably due, at least in part, to the increased number of prostate cells associated with these conditions and, therefore, that the levels of PSA can be indicative of a prostate cell proliferative disorder. Accordingly, Applicants submit that in the present case, one skilled in the art, viewing the specification and having knowledge of the art, would have known, for example, that increased levels of GDF-12 can be indicative of a liver cell proliferative disorder such as a hepatoma because GDF-12 is produced by liver cells and because it has been shown that increased levels of PSA, which is produced by prostate cells, is indicative of a prostate cell proliferative disorder.

In addition, it is noteworthy to mention that it is known that GDF-12 is expressed in liver cells but not in ovary, muscle, testis, spleen, intestine, pancreas, seminal vesicle, kidney, brain, thymus, lung or heart, as is set forth in Example 2 and Figure 1 of the application. It is also known that expression of GDF-12 increases with increased liver cell production. Accordingly, Applicants submit that evidence of a biological significance of the invention is disclosed by the specification.

In summary, it is submitted that the use of an antibody to determine the level of a protein in a sample from a subject, wherein the level of the protein is diagnostic of the proliferative or malignant state of the cells that produce the protein, is a well established utility, which is specific, substantial and credible, and that, in view of the subject application and of knowledge in the art such as the use of PSA levels as indicative of a prostate cell proliferative disorder, one skilled in the art clearly would have recognized that an antibody specific for GDF-12 can be used to determine levels of GDF-12, which can be indicative of malignant liver cells. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 15-18 under 35 U.S.C. § 112, first paragraph, as allegedly not being supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the rejection under 35 U.S.C. §101.

As set forth above, GDF-12 has the biological significance of increased expression with increased liver cell production. It is set forth that expression of GDF-12 is specific to liver cells. As GDF-12 is shown to have both structural and functional characteristics, and one of skill in the art would have been able to practice the invention at the time of filing, it is respectfully submitted that claims 15, 18-22 and 44-46 meet the requirements of 35 U.S.C. §112, first paragraph. Accordingly, removal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 15-18 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner alleges that claim 15 is vague because the method claim fails to recite steps. Applicants have amended claim 15 to recite specific steps for detecting malignant cells.

The Examiner further alleges that use of the term "having" in claim 15 is unclear. As suggested, Applicants have amended claim 15 to include the closed language "consisting of."

Finally, the Examiner alleges that there is insufficient antecedent basis for the limitation "cell" in claim 16. Applicants have amended claim 16 to recite "cells," which find antecedent basis in claim 15.

Accordingly, withdrawal of the rejections is respectfully requested.

Conclusion

In summary, for the reasons set forth herein, Applicants maintain that claims 15-18 clearly and patentably define the invention and respectfully request that the Examiner withdraw all rejections and pass the application to allowance. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Check No. 581383 is enclosed in the amount of $120.00 for the One-Month Petition for Extension of Time. The Commissioner is hereby authorized to charge any other fees that may be required by this paper or credit any overpayment to Deposit Account No. 07-1896 referencing the above-identified docket number. A duplicate copy of the Transmittal Sheet is attached.

Respectfully submitted,

Date: April 5, 2006

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